NMCP COVID-19 Literature Report #72: Friday, 16 July 2021

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Purpose: These reports, published every other week on Fridays, are curated collections of current research, evidence reviews, special reports, grey literature, and news regarding the COVID-19 pandemic that may be of interest to medical providers, leadership, and decision makers.

All reports are available online at https://nmcp.libguides.com/covidreport. Access is private; you will need to use the direct link or bookmark the URL.

Disclaimer: I am not a medical professional. This document is current as of the date noted above. While I make every effort to find and summarize available data, I cannot cover everything in the literature on COVID-19. Please feel free to reach out with questions, suggestions for future topics, or any other feedback.

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The Big Picture

News in Brief

Yet another grim milestone: On Wednesday, 07 July 2021, the global death toll for COVID-19 surpassed 4 million (USA Today).

"More than 90 people killed in fire at Iraqi hospital treating Covid-19 patients" (CNN).

"Pandemic-driven hunger is making the world more unequal" (WP; see also: UN report on world hunger and NMCP COVID-19 Lit Report #9 from 28 April 2020 for a summary on food insecurity).

"Gene hunters turn up new clues to help explain why Covid-19 hits some people so hard" (STAT; see also Nature article, included below).

Pandemic Origins

Long read: "From Wuhan to Paris to Milan, the search for 'patient zero'" (WP).

Meanwhile… "The World Health Organization said it will fix several 'unintended errors' in a joint report with China on the origins of the coronavirus crisis and will look into other possible discrepancies" (WP).

Literature and Information Sources

A new Surgeon General Advisory focuses on confronting health misinformation (HHS).

The latest supplement from *Clinical Infectious Diseases* is "A Snapshot of Work by the COVID-19 Public Health Response" (Clin Infect Dis).

"Scientists quit journal board, protesting 'grossly irresponsible' study claiming COVID-19 vaccines kill" (Science).

At the time of this writing, there have been 142 articles on COVID-19 retracted (RW).

Special Reports and Other Resources

G20 HLIP: A Global Deal for Our Pandemic Age (June 2021)

> "The High Level Independent Panel was asked by the G20 in January 2021 to propose how finance can be organized, systematically and sustainably, to reduce the world's vulnerability to future pandemics.
>
> Our report sets out critical and actionable solutions and investments to meet the challenge of an age of pandemics, and to avoid a repeat of the catastrophic damage that COVID-19 has brought. The Panel arrived at its recommendations after intensive deliberations and

> consultations with a wide range of stakeholders and experts around the globe over a period of four months. We urge that our proposals be discussed, developed further, and implemented as a matter of urgency."

Peer-Reviewed Articles

JAMA Netw Open: Guidance for Health Care Leaders During the Recovery Stage of the COVID-19 Pandemic: A Consensus Statement (08 July 2021)

> "Question What leadership imperatives are most essential for health leaders following the emergency stages of the COVID-19 pandemic?
>
> Findings In this consensus statement, 32 coauthors from 17 countries with expertise in various aspects of health leadership, health care, public health, and related fields outline 10 imperatives to guide leaders through recovery from the emergency stages of the pandemic. Key leadership capabilities and reflection questions are presented to guide leaders and to structure performance reviews.
>
> Meaning Leaders who most effectively implement this framework are ideally positioned to address urgent needs and inequalities in health systems and to cocreate a culture within their organizations that best serves its people."

Nature: Mapping the human genetic architecture of COVID-19 (08 July 2021)

> "The genetic makeup of an individual contributes to susceptibility and response to viral infection. While environmental, clinical and social factors play a role in exposure to SARS-CoV-2 and COVID-19 disease severity, host genetics may also be important. Identifying host-specific genetic factors may reveal biological mechanisms of therapeutic relevance and clarify causal relationships of modifiable environmental risk factors for SARS-CoV-2 infection and outcomes. We formed a global network of researchers to investigate the role of human genetics in SARS-CoV-2 infection and COVID-19 severity. We describe the results of three genome-wide association meta-analyses comprised of up to 49,562 COVID-19 patients from 46 studies across 19 countries. We reported 13 genome-wide significant loci that are associated with SARS-CoV-2 infection or severe manifestations of COVID-19. Several of these loci correspond to previously documented associations to lung or autoimmune and inflammatory diseases. They also represent potentially actionable mechanisms in response to infection. Mendelian Randomization analyses support a causal role for smoking and body mass index for severe COVID-19 although not for type II diabetes. The identification of novel host genetic factors associated with COVID-19, with unprecedented speed, was made possible by the community of human genetic researchers coming together to prioritize sharing of data, results, resources and analytical frameworks. This working model of

> international collaboration underscores what is possible for future genetic discoveries in emerging pandemics, or indeed for any complex human disease."

Ann Intern Med: Association Between Caseload Surge and COVID-19 Survival in 558 U.S. Hospitals, March to August 2020 (06 July 2021)

> "Background: Several U.S. hospitals had surges in COVID-19 caseload, but their effect on COVID-19 survival rates remains unclear, especially independent of temporal changes in survival.
>
> Objective: To determine the association between hospitals' severity-weighted COVID-19 caseload and COVID-19 mortality risk and identify effect modifiers of this relationship.
>
> Design: Retrospective cohort study. (ClinicalTrials.gov: NCT04688372).
>
> Setting: 558 U.S. hospitals in the Premier Healthcare Database.
>
> Participants: Adult COVID-19-coded inpatients admitted from March to August 2020 with discharge dispositions by October 2020.
>
> Measurements: Each hospital-month was stratified by percentile rank on a surge index (a severity-weighted measure of COVID-19 caseload relative to pre-COVID-19 bed capacity). The effect of surge index on risk-adjusted odds ratio (aOR) of in-hospital mortality or discharge to hospice was calculated using hierarchical modeling; interaction by surge attributes was assessed.
>
> Results: Of 144 116 inpatients with COVID-19 at 558 U.S. hospitals, 78 144 (54.2%) were admitted to hospitals in the top surge index decile. Overall, 25 344 (17.6%) died; crude COVID-19 mortality decreased over time across all surge index strata. However, compared with nonsurging (<50th surge index percentile) hospital-months, aORs in the 50th to 75th, 75th to 90th, 90th to 95th, 95th to 99th, and greater than 99th percentiles were 1.11 (95% CI, 1.01 to 1.23), 1.24 (CI, 1.12 to 1.38), 1.42 (CI, 1.27 to 1.60), 1.59 (CI, 1.41 to 1.80), and 2.00 (CI, 1.69 to 2.38), respectively. The surge index was associated with mortality across ward, intensive care unit, and intubated patients. The surge-mortality relationship was stronger in June to August than in March to May (slope difference, 0.10 [CI, 0.033 to 0.16]) despite greater corticosteroid use and more judicious intubation during later and higher-surging months. Nearly 1 in 4 COVID-19 deaths (5868 [CI, 3584 to 8171]; 23.2%) was potentially attributable to hospitals strained by surging caseload.
>
> Conclusion: Despite improvements in COVID-19 survival between March and August 2020, surges in hospital COVID-19 caseload remained detrimental to survival and potentially eroded benefits gained from emerging treatments. Bolstering preventive measures and supporting surging hospitals will save many lives."

SARS-CoV-2 Virus and Variants

News in Brief

"A woman died of COVID after contracting 2 variants at the same time, researchers say" (NPR; see also: ECCMID abstract [pdf] and press release).

"Despite new COVID variants, CDC says you don't need any booster doses right now" (NPR).

"Study highlights need for full Covid vaccination to protect against Delta variant" (STAT; see also: Nature article detailed below).

Long read: "What you need to know about the highly contagious delta variant: The variant first identified in India last year is now dominant in the United States" (WP).

Listen: "How the delta variant is changing the pandemic on a global scale" (NPR; ~15min).

Peer-Reviewed Articles

Clin Infect Dis: SARS-CoV-2 cumulative incidence, United States, August-December 2020 (10 July 2021)

> "Background: We conducted a national probability survey of US households to estimate the cumulative incidence adjusted for antibody waning.
>
> Methods: From August-December 2020, a multistage random sample of US addresses were mailed a survey and materials to self-collect nasal swabs and dried blood spots. One adult household member completed the survey and mail specimens for viral detection with PCR and total (IgA, IgM, IgG) nucleocapsid antibody by a commercial, EUA-approved antigen capture assay. We estimated cumulative incidence of SARS-CoV-2 adjusted for waning antibodies and calculated reported fraction and infection fatality ratio (IFR). Differences in seropositivity among demographic, geographic and clinical subgroups were explored with weighted prevalence ratios (PR).
>
> Results: Among 39,500 sampled households, 4,654 respondents provided responded. Cumulative incidence adjusted for waning was 11.9% (95% credible interval (CrI): 10.5-13.5%) as of October 30, 2020. We estimated 30,332,842 (CrI: 26,703,753- 34,335,338) total infections in the U.S. adult population by October 30, 2020. Reported fraction was 17% and IFR was 0.85% among adults. Non-Hispanic Black (PR: 2.2) and Hispanic (PR: 3.1) persons were more likely than White non-Hispanic to be seropositive, as were those living in metropolitan areas (PR: 2.5).
>
> Conclusions: One in 8 US adults had been infected with SARS-CoV-2 by late October 2020; but few had been accounted for in public health reporting. The scope of the COVID-19

> pandemic is likely substantially underestimated by reported cases. Disparities in COVID-19 by race observed among reported cases cannot be attributed to differential diagnosis or reporting of infections in some population subgroups."

Clin Infect Dis: Long-Term Persistence of Spike Antibody and Predictive Modeling of Antibody Dynamics Following Infection with SARS-CoV-2 (04 July 2021)

> "Methods: The Co-Stars study prospectively enrolled 3679 healthcare workers to comprehensively characterize the kinetics of SARS-CoV-2 spike (S), receptor-binding-domain (RBD) and nucleoprotein (N) antibodies in parallel. Participants screening seropositive had serial monthly serological testing for a maximum of 7 months with the Mesoscale Discovery Assay. Survival analysis determined the proportion of sero-reversion while two hierarchical Gamma models predicted the upper- and lower-bounds of long-term antibody trajectory.
>
> Results: A total of 1163 monthly samples were provided from 349 seropositive participants. At 200 days post-symptoms, >95% of participants had detectable S-antibodies compared to 75% with detectable N-antibodies. S-antibody was predicted to remain detectable in 95% of participants until 465 days [95%CI 370-575] using a 'continuous-decay' model and indefinitely using a 'decay-to-plateau' model to account for antibody secretion by long-lived plasma cells. S-antibody titers correlated strongly with surrogate neutralization in-vitro (R 2=0.72). N-antibodies, however, decayed rapidly with a half-life of 60 days [95%CI 52-68].
>
> Conclusions: The Co-STAR's study data presented here provides evidence for long-term persistence of neutralizing S-antibodies. This has important implications for the duration of functional immunity following SARS-CoV-2 infection. In contrast, the rapid decay of N-antibodies must be considered in future seroprevalence studies and public health decision-making. This is the first study to establish a mathematical framework capable of predicting long-term humoral dynamics following SARS-CoV-2 infection."

Nature: Reduced sensitivity of SARS-CoV-2 variant Delta to antibody neutralization (08 July 2021)

> "The SARS-CoV-2 B.1.617 lineage was identified in October 2020 in India. It has since then become dominant in some indian regions and UK and further spread to many countries. The lineage includes three main subtypes (B1.617.1, B.1.617.2 and B.1.617.3), harbouring diverse Spike mutations in the N-terminal domain (NTD) and the receptor binding domain (RBD) which may increase their immune evasion potential. B.1.617.2, also termed variant Delta, is believed to spread faster than other variants. Here, we isolated an infectious Delta strain from a traveller returning from India. We examined its sensitivity to monoclonal antibodies (mAbs) and to antibodies present in sera from COVID-19 convalescent individuals or vaccine recipients, in comparison to other viral strains. Variant Delta was resistant to neutralization by some anti-NTD and anti-RBD mAbs including Bamlanivimab, which were impaired in binding to the Spike. Sera from convalescent patients collected up to 12 months

> post symptoms were 4 fold less potent against variant Delta, relative to variant Alpha (B.1.1.7). Sera from individuals having received one dose of Pfizer or AstraZeneca vaccines barely inhibited variant Delta. Administration of two doses generated a neutralizing response in 95% of individuals, with titers 3 to 5 fold lower against Delta than Alpha. Thus, variant Delta spread is associated with an escape to antibodies targeting non-RBD and RBD Spike epitopes."

Science: Ultrapotent antibodies against diverse and highly transmissible SARS-CoV-2 variants (01 July 2021)

> "The emergence of highly transmissible SARS-CoV-2 variants of concern (VOC) that are resistant to therapeutic antibodies highlights the need for continuing discovery of broadly reactive antibodies. We identify four receptor-binding domain targeting antibodies from three early-outbreak convalescent donors with potent neutralizing activity against 23 variants including the B.1.1.7, B.1.351, P.1, B.1.429, B.1.526 and B.1.617 VOCs. Two antibodies are ultrapotent, with sub-nanomolar neutralization titers (IC50 0.3 to 11.1 ng/mL; IC80 1.5 to 34.5 ng/mL). We define the structural and functional determinants of binding for all four VOC-targeting antibodies and show that combinations of two antibodies decrease the in vitro generation of escape mutants, suggesting their potential in mitigating resistance development."

Vaccines and Vaccine Hesitancy

News in Brief

The FDA has issued a warning about Guillain-Barré syndrome in people who received the J&J COVID-19 vaccine (Medpage; see also: FDA letter).

"Tennessee is halting outreach on all vaccines for adolescents, including for Covid-19" (CNN; see also: this viewpoint from JAMA Pediatrics on vaccination of minors without parental consent).

Effectiveness

"Quarter-dose of Moderna COVID vaccine still rouses a big immune response: Results hint that dose stretching could help to address the world's acute vaccine shortage" (Nature).

"Immunized but banned: EU says not all COVID vaccines equal" (AP).

"Mounting evidence suggests Sputnik COVID vaccine is safe and effective: Russia's vaccine is in use in nearly 70 nations, but its adoption has been slowed by controversies and questions over rare side effects, and it has yet to garner World Health Organization approval" (Nature).

"Scientists identify long-sought marker for COVID vaccine success: Knowing which signatures in the blood predict protection against COVID-19 could speed the development of new vaccines" (Nature; see also: Coronapod podcast).

Boosters and Disparities

The CDC and FDA say people who are fully vaccinated "do not need a booster shot at this time" (HHS).

The head of the WHO says no one should be talking about booster shots anyway, not with so many around the world in need of COVID-19 vaccines (STAT).

Case in point: "COVID vaccines to reach poorest countries in 2023 — despite recent pledges: Amid a COVID surge in Africa, vaccine promises from richer nations are not enough to bring an early end to the pandemic, experts say" (Nature).

Hesitancy

"15 million people in the U.S. have missed their second dose of the coronavirus vaccine, CDC says" (WP).

"Experts warn full Covid-19 vaccine approval is no quick fix for hesitancy" (STAT).

"They didn't want to get Covid-19 shots. This is what convinced them. From encouragement from family to fears over new variants, this is what swayed vaccine holdouts" (NBC).

For some communities of color, it may help to partner with religious leaders and pharmacists to increase vaccine uptake (EurekAlert; see also: ECCMID abstract).

According to a new poll: "Being concerned about side effects is the top reason offered by unvaccinated people for why they haven't gotten a COVID-19 vaccine. When asked what would motivate them to get vaccinated against COVID-19, most in the 'wait and see' group say they just want more time to see how the vaccine affects others who have already gotten it" (KFF).

Other Vaccine News

"First nurse to receive COVID-19 vaccine will have her scrubs and vaccine card displayed in Smithsonian" (CBS).

Mountain lions and tigers and bears, oh my! "Oakland Zoo begins experimental COVID-19 vaccine program on its wildlife: Tigers, bears, mountain lions and ferrets were the first to get the vaccine" (ABC).

Special Reports and Other Resources

JHCHS: Carrying Equity in COVID-19 Vaccination Forward: Guidance Informed by Communities of Color (14 July 2021)

> "Seven months into the COVID-19 vaccination campaign in the United States, nearly 50% of the American population has been vaccinated. While this is a monumental accomplishment, there is still much work to do.
>
> In the coming months, the country will face a series of vaccination challenges including serving groups with persistently low vaccine uptake (due to, for example, low/no access, vaccine hesitancy, or a combination of factors), expanding COVID-19 vaccination to children (particularly those whose parents may be less willing to vaccinate their children than to get vaccinated themselves), and orchestrating a potential booster dose campaign (with its own hesitancy issues). As the COVID-19 vaccination campaign continues, lessons from the vaccine rollout to date can help provide direction moving forward.
>
> One challenge that deserves closer attention and more refined solutions is the campaign's limited success at delivering vaccines to low-income persons and communities of color. During the pandemic, these populations have experienced significant physical, financial, and psychological harms at a disproportionate rate. The continued emergence and spread of new SARS-CoV-2 virus variants and the resumption of routine social, commercial, and educational activities across the country amplify the risks that COVID-19 poses to these groups.
>
> This report provides specific guidance on adapting COVID-19 vaccination efforts to achieve greater vaccine coverage in underserved populations and, through this, to develop sustainable, locally appropriate mechanisms to advance equity in health.
>
> In the first half of the report, we outline findings from local, ethnographic research conducted within Black and Hispanic/Latino communities in Alabama, California, Idaho, Maryland, and Virginia. Since January, local research teams have been assessing community infrastructure; listening to community members, public health officials, and government leaders; and coordinating engagement activities to understand how best to promote awareness of, access to, and acceptability of COVID-19 vaccines. In the second half of this report, we present the policy and practice implications of the local research. The Working Group on Equity in COVID-19 Vaccination—an advisory body of community advocates, public health experts, and social scientists—developed the recommendations, eliciting local team feedback."

Commonwealth Fund: Deaths and Hospitalizations Averted by Rapid U.S. Vaccination Rollout (07 July 2021)

> "The COVID-19 pandemic has unleashed devastating health and economic crises worldwide, causing more than 3.9 million deaths and 183 million reported infections globally. While the United States has accounted for more than 600,000 deaths, it also has supported the development of highly efficacious vaccines, granting emergency authorizations and delivering the products at an unprecedented pace. As of July 2, the U.S. had administered more than 328 million vaccine doses, with 67 percent of adults having received at least one dose. The number of cases has fallen from more than 300,000 per day at the apex of the pandemic in January 2021 to less than 20,000 per day in mid-June….
>
> To assess the impact of the U.S. vaccination program, we expanded our age-stratified, agent-based model of COVID-19 to include transmission dynamics of the Alpha, Gamma, and Delta variants in addition to the original Wuhan-1 variant. (For details, see How We Conducted This Study). Briefly, the model compared the observed epidemiologic trajectory (cases, hospitalizations, and deaths) to two counterfactual scenarios, one in which no vaccination program occurred and another under which daily vaccinations were administered at only half the actual daily pace.
>
> Highlights
>
> - Without a vaccination program, by the end of June 2021 there would have been approximately 279,000 additional deaths and up to 1.25 million additional hospitalizations.
> - If the U.S. had achieved only half the actual pace of vaccination, there would have been nearly 121,000 additional deaths and more than 450,000 additional hospitalizations.
> - If there had been no vaccination program, daily deaths from COVID-19 potentially would have jumped to nearly 4,500 deaths per day during a second "2021 spring surge" — eclipsing the observed daily peak of 4,000 during the first 2021 winter surge."

Peer-Reviewed Articles

Administration and Coverage

MMWR: COVID-19 Vaccination Coverage Among Insured Persons Aged ≥16 Years, by Race/Ethnicity and Other Selected Characteristics — Eight Integrated Health Care Organizations, United States, December 14, 2020–May 15, 2021 (16 July 2021)

> "What is already known about this topic? Non-Hispanic Black and Hispanic persons experience higher COVID-19–associated morbidity and mortality, yet COVID-19 vaccination coverage is lower in these groups.

> What is added by this report? As of May 15, 2021, 48.3% of persons identified in CDC's Vaccine Safety Datalink aged ≥16 years had received ≥1 COVID-19 vaccine dose and 38.3% were fully vaccinated. Coverage with ≥1 dose was lower among non-Hispanic Black (40.7%) and Hispanic persons (41.1%) than among non-Hispanic White persons (54.6%); coverage was highest (57.4%) among non-Hispanic Asian persons.
>
> What are the implications for public health practice? Continued monitoring of vaccination coverage and efforts to improve equity in vaccination coverage are critical, especially among populations disproportionately affected by COVID-19."

MMWR: COVID-19 Vaccine Administration, by Race and Ethnicity — North Carolina, December 14, 2020–April 6, 2021 (16 July 2021)

> "What is already known about this topic? COVID-19 has disproportionately affected Black or African American and Hispanic communities.
>
> What is added by this report? Among persons vaccinated during March 29–April 6, 2021, compared with December 14, 2020–January 3, 2021, in North Carolina, the proportion who were Black nearly doubled, and the share of vaccine doses administered to Hispanic persons doubled during this period, approaching the proportion of the state population for these groups aged ≥16 years.
>
> What are the implications for public health practice? To promote equitable vaccination coverage, public health officials could consider using U.S. Census tract-level mapping to guide vaccine allocation, promote shared accountability for equitable distribution of vaccines with providers through data sharing, and facilitate community partnerships to support vaccine access."

MMWR: Acceptability of Adolescent COVID-19 Vaccination Among Adolescents and Parents of Adolescents — United States, April 15–23, 2021 (09 July 2021)

> "What is already known about this topic? Pfizer-BioNTech's COVID-19 vaccine was authorized by the Food and Drug Administration and recommended by the Advisory Committee on Immunization Practices in May 2021 for adolescents aged 12–15 years.
>
> What is added by this report? In April 2021, 52% of unvaccinated adolescents aged 13–17 years and 56% of parents of unvaccinated adolescents aged 12–17 years reported intent for adolescent COVID-19 vaccination. The most common factors that would increase vaccination intent were receiving more information about adolescent COVID-19 vaccine safety and efficacy.
>
> What are the implications for public health practice? Efforts focusing on effectively communicating the benefits and safety of COVID-19 vaccination for adolescents to the

> public could help increase adolescent COVID-19 vaccine confidence and vaccination coverage."

JAMA Netw Open: Asymptomatic and Symptomatic COVID-19 Infections Among Health Care Personnel Before and After Vaccination (08 July 2021)

> "This cohort study investigates asymptomatic and symptomatic COVID-19 case rates before and after the initial vaccine rollout among health care personnel in Orange County, California."

Efficacy

Clin Infect Dis: Evaluating Vaccine Efficacy Against SARS-CoV-2 Infection (14 July 2021)

> "Although interim results from several large placebo-controlled phase 3 trials demonstrated high vaccine efficacy (VE) against symptomatic COVID-19, it is unknown how effective the vaccines are in preventing people from becoming asymptomatically in- fected and potentially spreading the virus unwittingly. It is more difficult to evaluate VE against SARS-CoV-2 infection than against symptomatic COVID-19 because infection is not observed directly but rather is known to occur between two antibody or RT-PCR tests. Ad- ditional challenges arise as community transmission changes over time and as participants are vaccinated on different dates because of staggered enrollment of participants or crossover of placebo recipients to the vaccine arm before the end of the study. Here, we provide valid and efficient statistical methods for estimating potentially waning VE against SARS-CoV-2 infection with blood or nasal samples under time-varying community transmission, staggered enrollment, and blinded or unblinded crossover. We demonstrate the usefulness of the proposed methods through numerical studies mimicking the BNT162b2 phase 3 trial and the Prevent COVID U study. In addition, we assess how crossover and the frequency of diagnostic tests affect the precision of VE estimates."

Clin Infect Dis: Single-dose mRNA vaccine effectiveness against SARS-CoV-2, including Alpha and Gamma variants: a test-negative design in adults 70 years and older in British Columbia, Canada (09 July 2021)

> "Introduction: Randomized-controlled trials of mRNA vaccine protection against SARS-CoV-2 included few elderly participants. We assess single-dose mRNA vaccine effectiveness (VE) in adults ≥70-years-old in British Columbia (BC), Canada where second doses were deferred by up to 16 weeks and where a spring 2021 wave uniquely included co-dominant circulation of Alpha (B.1.1.7) and Gamma (P.1) variants of concern (VOC).
>
> Methods: Analyses included community-dwelling adults ≥70-years-old with specimen collection between April 4 (epidemiological week 14) and May 1 (week 17) 2021. Adjusted VE was estimated by test-negative design. Cases were RT-PCR test-positive for SARS-CoV-2 and controls were test-negative. Vaccine status was defined by receipt of a single-dose ≥21

> days before specimen collection, but a range of intervals was assessed. Variant-specific VE was estimated against viruses genetically characterized as Alpha, Gamma or non-VOC lineages.
>
> Results: VE analyses included 16,993 specimens: 1,226 (7.2%) test-positive cases and 15,767 test-negative controls. Of 1,131 (92%) genetically-characterized viruses, 509 (45%), 314 (28%) and 276 (24%) were Alpha, Gamma and non-VOC lineages, respectively. At 0-13 days post-vaccination, VE was negligible at 14% (95% CI 0-26) but increased from 43% (95% CI 30-53) at 14-20 days to 75% (95% CI 63-83) at 35-41 days post-vaccination. VE at ≥21 days post-vaccination was 65% (95% CI 58-71) overall: 72% (95% CI 58-81), 67% (95% CI 57-75) and 61% (95% CI 45-72) for non-VOC, Alpha and Gamma variants, respectively.
>
> Conclusions: A single dose of mRNA vaccine reduced the risk of SARS-CoV-2 by about two-thirds in adults ≥70-years-old, with protection only minimally reduced against Alpha and Gamma variants."

Lancet: Efficacy and safety of an inactivated whole-virion SARS-CoV-2 vaccine (CoronaVac): interim results of a double-blind, randomised, placebo-controlled, phase 3 trial in Turkey (08 July 2021)

> "Background: CoronaVac, an inactivated whole-virion SARS-CoV-2 vaccine, has been shown to be well tolerated with a good safety profile in individuals aged 18 years and older in phase 1/2 trials, and provided a good humoral response against SARS-CoV-2. We present the interim efficacy and safety results of a phase 3 clinical trial of CoronaVac in Turkey.
>
> Methods: This was a double-blind, randomised, placebo-controlled phase 3 trial. Volunteers aged 18-59 years with no history of COVID-19 and with negative PCR and antibody test results for SARS-CoV-2 were enrolled at 24 centres in Turkey. Exclusion criteria included (but were not limited to) immunosuppressive therapy (including steroids) within the past 6 months, bleeding disorders, asplenia, and receipt of any blood products or immunoglobulins within the past 3 months. The K1 cohort consisted of health-care workers (randomised in a 1:1 ratio), and individuals other than health-care workers were also recruited into the K2 cohort (randomised in a 2:1 ratio) using an interactive web response system. The study vaccine was 3 μg inactivated SARS-CoV-2 virion adsorbed to aluminium hydroxide in a 0·5 mL aqueous suspension. Participants received either vaccine or placebo (consisting of all vaccine components except inactivated virus) intramuscularly on days 0 and 14. The primary efficacy outcome was the prevention of PCR-confirmed symptomatic COVID-19 at least 14 days after the second dose in the per protocol population. Safety analyses were done in the intention-to-treat population. This study is registered with ClinicalTrials.gov (NCT04582344) and is active but no longer recruiting.
>
> Findings: Among 11 303 volunteers screened between Sept 14, 2020, and Jan 5, 2021, 10 218 were randomly allocated. After exclusion of four participants from the vaccine group

> because of protocol deviations, the intention-to-treat group consisted of 10 214 participants (6646 [65·1%] in the vaccine group and 3568 [34·9%] in the placebo group) and the per protocol group consisted of 10 029 participants (6559 [65·4%] and 3470 [34·6%]) who received two doses of vaccine or placebo. During a median follow-up period of 43 days (IQR 36-48), nine cases of PCR-confirmed symptomatic COVID-19 were reported in the vaccine group (31·7 cases [14·6-59·3] per 1000 person-years) and 32 cases were reported in the placebo group (192·3 cases [135·7-261·1] per 1000 person-years) 14 days or more after the second dose, yielding a vaccine efficacy of 83·5% (95% CI 65·4-92·1; p<0·0001). The frequencies of any adverse events were 1259 (18·9%) in the vaccine group and 603 (16·9%) in the placebo group (p=0·0108) with no fatalities or grade 4 adverse events. The most common systemic adverse event was fatigue (546 [8·2%] participants in the vaccine group and 248 [7·0%] the placebo group, p=0·0228). Injection-site pain was the most frequent local adverse event (157 [2·4%] in the vaccine group and 40 [1·1%] in the placebo group, p<0·0001).
>
> Interpretation: CoronaVac has high efficacy against PCR-confirmed symptomatic COVID-19 with a good safety and tolerability profile."

NEJM: Effectiveness of an Inactivated SARS-CoV-2 Vaccine in Chile (07 July 2021)

> "Background: Mass vaccination campaigns to prevent coronavirus disease 2019 (Covid-19) are occurring in many countries; estimates of vaccine effectiveness are urgently needed to support decision making. A countrywide mass vaccination campaign with the use of an inactivated severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccine (CoronaVac) was conducted in Chile starting on February 2, 2021.
>
> Methods: We used a prospective national cohort, including participants 16 years of age or older who were affiliated with the public national health care system, to assess the effectiveness of the inactivated SARS-CoV-2 vaccine with regard to preventing Covid-19 and related hospitalization, admission to the intensive care unit (ICU), and death. We estimated hazard ratios using the extension of the Cox proportional-hazards model, accounting for time-varying vaccination status. We estimated the change in the hazard ratio associated with partial immunization (≥14 days after receipt of the first dose and before receipt of the second dose) and full immunization (≥14 days after receipt of the second dose). Vaccine effectiveness was estimated with adjustment for individual demographic and clinical characteristics.
>
> Results: The study was conducted from February 2 through May 1, 2021, and the cohort included approximately 10.2 million persons. Among persons who were fully immunized, the adjusted vaccine effectiveness was 65.9% (95% confidence interval [CI], 65.2 to 66.6) for the prevention of Covid-19 and 87.5% (95% CI, 86.7 to 88.2) for the prevention of

> hospitalization, 90.3% (95% CI, 89.1 to 91.4) for the prevention of ICU admission, and 86.3% (95% CI, 84.5 to 87.9) for the prevention of Covid-19-related death.
>
> Conclusions: Our results suggest that the inactivated SARS-CoV-2 vaccine effectively prevented Covid-19, including severe disease and death, a finding that is consistent with results of phase 2 trials of the vaccine."

Adverse Events

MMWR: Use of mRNA COVID-19 Vaccine After Reports of Myocarditis Among Vaccine Recipients: Update from the Advisory Committee on Immunization Practices — United States, June 2021 (09 July 2021)

> "What is already known about this topic? An elevated risk for myocarditis among mRNA COVID-19 vaccinees has been observed, particularly in males aged 12–29 years.
>
> What is added by this report? On June 23, 2021, the Advisory Committee on Immunization Practices concluded that the benefits of COVID-19 vaccination to individual persons and at the population level clearly outweighed the risks of myocarditis after vaccination.
>
> What are the implications for public health practice? Continued use of mRNA COVID-19 vaccines in all recommended age groups will prevent morbidity and mortality from COVID-19 that far exceed the number of cases of myocarditis expected. Information regarding the risk for myocarditis with mRNA COVID-19 vaccines should be disseminated to providers to share with vaccine recipients."

Nature: Antibody epitopes in vaccine-induced immune thrombotic thrombocytopenia (07 July 2021)

> "Vaccine-induced immune thrombotic thrombocytopenia (VITT) is a rare adverse effect of COVID-19 adenoviral vector vaccines. VITT resembles heparin-induced thrombocytopenia (HIT) as it is associated with platelet-activating antibodies against platelet factor 4 (PF4); however, patients with VITT develop thrombocytopenia and thrombosis without heparin exposure. The objective of this study was to determine the binding site on PF4 of antibodies from patients with VITT. Using alanine scanning mutagenesis, we determined the binding of VITT anti-PF4 antibodies (n=5) was restricted to 8 surface amino acids, all of which were located within the heparin binding site on PF4, and the binding was inhibited by heparin. In contrast, HIT sampled (n=10) bound to amino acids corresponding to 2 different sites on PF4. Using biolayer interferometry, we demonstrated VITT anti-PF4 antibodies had a stronger binding response against PF4 and PF4/heparin complexes than HIT antibodies; albeit, with similar dissociation rates. Our data indicates VITT antibodies can mimic the effect of heparin by binding to a similar site on PF4, allowing PF4 tetramers to cluster and form immune complexes, which in turn cause FcγRIIa-dependent platelet activation. These

> results provide an explanation for VITT antibody-induced platelet activation that could contribute to thrombosis."

Hesitancy

JAMA: Lottery-Based Incentive in Ohio and COVID-19 Vaccination Rates (02 July 2021)

> "This study assesses changes in COVID-19 vaccination rates before and after the Ohio vaccine lottery announcement compared with national rates to control for the expansion of vaccine indications to adolescents."

Treatments and Management

News in Brief

ASPR had developed a new tool, the COVID-19 Monoclonal Antibody Therapeutics Calculator, to help manage and reduce COVID-19 surges (PHE).

Peer-Reviewed Articles

Lancet: Characterisation of in-hospital complications associated with COVID-19 using the ISARIC WHO Clinical Characterisation Protocol UK: a prospective, multicentre cohort study (17 July 2021)

> "Background COVID-19 is a multisystem disease and patients who survive might have in-hospital complications. These complications are likely to have important short-term and long-term consequences for patients, health-care utilisation, health-care system preparedness, and society amidst the ongoing COVID-19 pandemic. Our aim was to characterise the extent and effect of COVID-19 complications, particularly in those who survive, using the International Severe Acute Respiratory and Emerging Infections Consortium WHO Clinical Characterisation Protocol UK.
>
> Methods We did a prospective, multicentre cohort study in 302 UK health-care facilities. Adult patients aged 19 years or older, with confirmed or highly suspected SARS-CoV-2 infection leading to COVID-19 were included in the study. The primary outcome of this study was the incidence of in-hospital complications, defined as organ-specific diagnoses occurring alone or in addition to any hallmarks of COVID-19 illness. We used multilevel logistic regression and survival models to explore associations between these outcomes and in-hospital complications, age, and pre-existing comorbidities.

> Findings Between Jan 17 and Aug 4, 2020, 80 388 patients were included in the study. Of the patients admitted to hospital for management of COVID-19, 49·7% (36 367 of 73 197) had at least one complication. The mean age of our cohort was 71·1 years (SD 18·7), with 56·0% (41 025 of 73 197) being male and 81·0% (59 289 of 73 197) having at least one comorbidity. Males and those aged older than 60 years were most likely to have a complication (aged ≥60 years: 54·5% [16 579 of 30 416] in males and 48·2% [11 707 of 24 288] in females; aged <60 years: 48·8% [5179 of 10 609] in males and 36·6% [2814 of 7689] in females). Renal (24·3%, 17 752 of 73 197), complex respiratory (18·4%, 13 486 of 73 197), and systemic (16·3%, 11 895 of 73 197) complications were the most frequent. Cardiovascular (12·3%, 8973 of 73 197), neurological (4·3%, 3115 of 73 197), and gastrointestinal or liver (0·8%, 7901 of 73 197) complications were also reported.
>
> Interpretation Complications and worse functional outcomes in patients admitted to hospital with COVID-19 are high, even in young, previously healthy individuals. Acute complications are associated with reduced ability to self-care at discharge, with neurological complications being associated with the worst functional outcomes. COVID-19 complications are likely to cause a substantial strain on health and social care in the coming years. These data will help in the design and provision of services aimed at the post-hospitalisation care of patients with COVID-19."

Clin Infect Dis: Clinical improvement, outcomes, antiviral activity, and costs associated with early treatment with remdesivir for patients with COVID-19 (15 July 2021)

> "Background: Evidence remains inconclusive on any significant benefits of remdesivir in mild-to-moderate COVID-19 patients. This study explored the disease progression, various clinical outcomes, changes in viral load, and costs associated with early remdesivir treatment among COVID-19 patients.
>
> Methods: A territory-wide retrospective cohort of 10,419 patients with COVID-19 hospitalized from 21st January 2020 to 31st January 2021 in Hong Kong were identified. Early remdesivir users were matched with controls using propensity-score matching in a ratio of up to 1:4. Study outcomes were time to clinical improvement on the WHO clinical progression scale of at least 1 score; hospital discharge; recovery; viral clearance; low viral load; positive IgG antibody; in-hospital death; and composite outcomes of in-hospital death, requiring invasive ventilation or intensive care.
>
> Results: After multiple imputation and propensity-score matching, the median follow-up was 14 days for both remdesivir (n=352) and control (n=1,347) groups. Time to clinical improvement was significantly shorter in the remdesivir group than that of control (hazard ratio (HR)=1.14, 95%CI 1.01-1.29, p=0.038), as well as for achieving low viral load (HR=1.51, 95%CI 1.24-1.83, p<0.001) and positive IgG antibody (HR=1.50, 95%CI 1.31-1.70, p<0.001). Early remdesivir treatment was associated with a lower risk of in-hospital death (HR=0.58,

> 95%CI 0.34-0.99, p=0.045), in addition to a significantly shorter length of hospital stay (difference -2.56 days, 95%CI -4.86 to -0.26, p=0.029), without increasing the risks of composite outcomes for clinical deterioration.
>
> Conclusions: Early remdesivir treatment could be extended to hospitalized patients presenting with moderate COVID-19 and not requiring oxygen therapy on admission."

NEJM: Bamlanivimab plus Etesevimab in Mild or Moderate Covid-19 (14 July 2021)

> "Background: Patients with underlying medical conditions are at increased risk for severe coronavirus disease 2019 (Covid-19). Whereas vaccine-derived immunity develops over time, neutralizing monoclonal-antibody treatment provides immediate, passive immunity and may limit disease progression and complications.
>
> Methods: In this phase 3 trial, we randomly assigned, in a 1:1 ratio, a cohort of ambulatory patients with mild or moderate Covid-19 who were at high risk for progression to severe disease to receive a single intravenous infusion of either a neutralizing monoclonal-antibody combination agent (2800 mg of bamlanivimab and 2800 mg of etesevimab, administered together) or placebo within 3 days after a laboratory diagnosis of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. The primary outcome was the overall clinical status of the patients, defined as Covid-19-related hospitalization or death from any cause by day 29.
>
> Results: A total of 1035 patients underwent randomization and received an infusion of bamlanivimab-etesevimab or placebo. The mean (±SD) age of the patients was 53.8±16.8 years, and 52.0% were adolescent girls or women. By day 29, a total of 11 of 518 patients (2.1%) in the bamlanivimab-etesevimab group had a Covid-19-related hospitalization or death from any cause, as compared with 36 of 517 patients (7.0%) in the placebo group (absolute risk difference, -4.8 percentage points; 95% confidence interval [CI], -7.4 to -2.3; relative risk difference, 70%; P<0.001). No deaths occurred in the bamlanivimab-etesevimab group; in the placebo group, 10 deaths occurred, 9 of which were designated by the trial investigators as Covid-19-related. At day 7, a greater reduction from baseline in the log viral load was observed among patients who received bamlanivimab plus etesevimab than among those who received placebo (difference from placebo in the change from baseline, -1.20; 95% CI, -1.46 to -0.94; P<0.001).
>
> Conclusions: Among high-risk ambulatory patients, bamlanivimab plus etesevimab led to a lower incidence of Covid-19-related hospitalization and death than did placebo and accelerated the decline in the SARS-CoV-2 viral load."

Ann Intern Med: Evaluation of the Effects of Remdesivir and Hydroxychloroquine on Viral Clearance in COVID-19 (13 July 2021)

> "Background: New treatment modalities are urgently needed for patients with COVID-19. The World Health Organization (WHO) Solidarity trial showed no effect of remdesivir or hydroxychloroquine (HCQ) on mortality, but the antiviral effects of these drugs are not known.
>
> Objective: To evaluate the effects of remdesivir and HCQ on all-cause, in-hospital mortality; the degree of respiratory failure and inflammation; and viral clearance in the oropharynx.
>
> Setting: 23 hospitals in Norway.
>
> Patients: Eligible patients were adults hospitalized with confirmed SARS-CoV-2 infection.
>
> Intervention: Between 28 March and 4 October 2020, a total of 185 patients were randomly assigned and 181 were included in the full analysis set. Patients received remdesivir (n = 42), HCQ (n = 52), or standard of care (SoC) (n = 87).
>
> Measurements: In addition to the primary end point of WHO Solidarity, study-specific outcomes were viral clearance in oropharyngeal specimens, the degree of respiratory failure, and inflammatory variables.
>
> Results: No significant differences were seen between treatment groups in mortality during hospitalization. There was a marked decrease in SARS-CoV-2 load in the oropharynx during the first week overall, with similar decreases and 10-day viral loads among the remdesivir, HCQ, and SoC groups. Remdesivir and HCQ did not affect the degree of respiratory failure or inflammatory variables in plasma or serum. The lack of antiviral effect was not associated with symptom duration, level of viral load, degree of inflammation, or presence of antibodies against SARS-CoV-2 at hospital admittance.
>
> Limitation: The trial had no placebo group.
>
> Conclusion: Neither remdesivir nor HCQ affected viral clearance in hospitalized patients with COVID-19."

JAMA Netw Open: Clinical Characterization and Prediction of Clinical Severity of SARS-CoV-2 Infection Among US Adults Using Data From the US National COVID Cohort Collaborative (13 July 2021)

> "Question In a US data resource large enough to adjust for multiple confounders, what risk factors are associated with COVID-19 severity and severity trajectory over time, and can machine learning models predict clinical severity?
>
> Findings In this cohort study of 174 568 adults with SARS-CoV-2, 32 472 (18.6%) were hospitalized and 6565 (20.2%) were severely ill, and first-day machine learning models

> accurately predicted clinical severity. Mortality was 11.6% overall and decreased from 16.4% in March to April 2020 to 8.6% in September to October 2020.
>
> Meaning These findings suggest that machine learning models can be used to predict COVID-19 clinical severity with the use of an available large-scale US COVID-19 data resource."

Radiology: Pulmonary Embolism in Hospitalized Patients with COVID-19: A Multicenter Study (13 July 2021)

> "Background Pulmonary embolism (PE) commonly complicates SARS-CoV-2 infection but there is heterogeneity in incidence and mortality in the single center reports and risk factors.
>
> Purpose To determine the incidence of PE in COVID-19 and its associations with clinical and laboratory parameters.
>
> Methods Electronic medical records were searched retrospectively for demographic, clinical and laboratory data and outcomes in patients admitted with COVID-19 at 4 hospitals March-June 2020. PE on CT pulmonary angiography (CTPA) and perfusion scintigraphy was correlated with clinical and laboratory parameters. D-dimer was used to predict PE and the obtained threshold underwent an external validation on 85 hospitalized patients with COVID-19 at a 5th hospital. We also assessed the association between right heart strain and embolic burden in patients with PE undergoing echocardiography.
>
> Results Four-hundred-thirteen patients with COVID-19 (230 men, aged 20-98 years, mean + SD = 60+16 years) were evaluated. PE was diagnosed in 25% (102/413, 95%CI: 21%-29%) of hospitalized patients with COVID-19, undergoing CTPA or perfusion scintigraphy. PE was observed in 29% (21/73, 95%CI:19% -41%) of ICU vs. 24% (81/340, 95%CI:20% -29%) of non-ICU patients (p=0.37). PE was associated with male sex(Odds Ratio=OR[95% CI]: 1.7[1.1-2.8], p=0.02), smoking (OR[95% CI]:1.8[1.01-3.4], p=0.04) and increased d-dimer (p<0.001), lactate dehydrogenase (p<0.001), ferritin (p=0.001) and IL-6 (p=0.02). Mortality in hospitalized patients was similar between those with PE and without PE (14%[13/102, 95%CI: 8% - 22%]vs 13%[40/311, 95%CI: 9% - 17%], p=0.98), suggesting that diagnosis and treatment of PE was not associated with excess mortality. D-dimer>1600 ng/mL predicts PE with 100% sensitivity and 62% specificity in an external validation cohort. Embolic burden was higher in patients with right heart strain among the patients with PE undergoing echocardiogram (p=0.03).
>
> Conclusion Pulmonary embolism incidence was 25% in patients hospitalized with COVID-19 suspected of PE. D-dimer>1600ng/mL was sensitive for identifying which patients need CTPA."
>
> See also: editorial

Clin Infect Dis: Fecal SARS-CoV-2 RNA is associated with decreased COVID-19 survival (10 July 2021)

> "The clinical significance of SARS CoV-2 RNA in stool remains uncertain. We found that extrapulmonary dissemination of infection to the gastrointestinal (GI) tract, assessed by the presence of SARS-CoV-2 RNA in stool, is associated with decreased COVID-19 survival. Measurement of SARS-CoV-2 RNA in stool may have utility for clinical risk assessment."

Lancet Respir Med: Azithromycin versus standard care in patients with mild-to-moderate COVID-19 (ATOMIC2): an open-label, randomised trial (09 July 2021)

> "Background: The antibacterial, anti-inflammatory, and antiviral properties of azithromycin suggest therapeutic potential against COVID-19. Randomised data in mild-to-moderate disease are not available. We assessed whether azithromycin is effective in reducing hospital admission in patients with mild-to-moderate COVID-19.
>
> Methods: This prospective, open-label, randomised superiority trial was done at 19 hospitals in the UK. We enrolled adults aged at least 18 years presenting to hospitals with clinically diagnosed, highly probable or confirmed COVID-19 infection, with fewer than 14 days of symptoms, who were considered suitable for initial ambulatory management. Patients were randomly assigned (1:1) to azithromycin (500 mg once daily orally for 14 days) plus standard care or to standard care alone. The primary outcome was death or hospital admission from any cause over the 28 days from randomisation. The primary and safety outcomes were assessed according to the intention-to-treat principle. This trial is registered at ClinicalTrials.gov (NCT04381962) and recruitment is closed.
>
> Findings: 298 participants were enrolled from June 3, 2020, to Jan 29, 2021. Three participants withdrew consent and requested removal of all data, and three further participants withdrew consent after randomisation, thus, the primary outcome was assessed in 292 participants (145 in the azithromycin group and 147 in the standard care group). The mean age of the participants was 45·9 years (SD 14·9). 15 (10%) participants in the azithromycin group and 17 (12%) in the standard care group were admitted to hospital or died during the study (adjusted OR 0·91 [95% CI 0·43-1·92], p=0·80). No serious adverse events were reported.
>
> Interpretation: In patients with mild-to-moderate COVID-19 managed without hospital admission, adding azithromycin to standard care treatment did not reduce the risk of subsequent hospital admission or death. Our findings do not support the use of azithromycin in patients with mild-to-moderate COVID-19."

JAMA: Association Between Administration of IL-6 Antagonists and Mortality Among Patients Hospitalized for COVID-19: A Meta-analysis (06 July 2021)

> "Question Is administration of IL-6 antagonists associated with 28-day all-cause mortality in patients hospitalized for COVID-19?
>
> Findings This prospective meta-analysis of 27 randomized trials included 10 930 patients, of whom 2565 died by 28 days. The 28-day all-cause mortality was lower among patients who received IL-6 antagonists compared with those who received usual care or placebo (summary odds ratio, 0.86). The summary odds ratios for the association of IL-6 antagonist treatment with 28-day all-cause mortality were 0.78 with concomitant administration of corticosteroids vs 1.09 without administration of corticosteroids.
>
> Meaning Administration of IL-6 antagonists, compared with usual care or placebo, was associated with lower 28-day all-cause mortality in patients hospitalized for COVID-19."

Open Forum Infect Dis: Meta-analysis of randomized trials of ivermectin to treat SARS-CoV-2 infection (06 July 2021)

> "Ivermectin is an antiparasitic drug being investigated for repurposing against SARS-CoV-2. Ivermectin showed in-vitro activity against SARS-COV-2 at high concentrations. This meta-analysis investigated ivermectin in 24 randomized clinical trials (3328 patients) identified through systematic searches of PUBMED, EMBASE, MedRxiv and trial registries. Ivermectin was associated with reduced inflammatory markers (C-Reactive Protein, d-dimer and ferritin) and faster viral clearance by PCR. Viral clearance was treatment dose- and duration-dependent. In 11 randomized trials of moderate/severe infection, there was a 56% reduction in mortality (Relative Risk 0.44 [95%CI 0.25-0.77]; p=0.004; 35/1064 (3%) deaths on ivermectin; 93/1063 (9%) deaths in controls) with favorable clinical recovery and reduced hospitalization. Many studies included were not peer reviewed and a wide range of doses were evaluated. Currently, WHO recommends the use of ivermectin only inside clinical trials. A network of large clinical trials is in progress to validate the results seen to date."

Pre-Existing Conditions, Comorbidities, and Impact on Other Diseases

News in Brief

"COVID and the brain: researchers zero in on how damage occurs: Growing evidence suggests that the coronavirus causes 'brain fog' and other neurological symptoms through multiple mechanisms" (Nature).

"Doctors might have been focusing on the wrong asthma triggers: The pandemic was a big social experiment that sent asthma attacks plummeting" (Atlantic).

Special Reports and Other Resources

NCI: Annual Report to the Nation on the Status of Cancer (08 July 2021)
NB: This report, which not specific to COVID-19, is included because of its potential value.

> "The Annual Report to the Nation on the Status of Cancer (ARN) is an update of rates for new cases and deaths as well as trends for the most common cancers in the United States. ARN provides rates and trends for the most common cancers among adults, children (aged 0-14), and adolescents and young adults or AYAs (aged 15-39).
>
> The report includes long-term trends (since 2001) and short-term trends with the most recent five years of data (2013-2017 for incidence and 2014-2018 for mortality).
>
> Key points:
>
> - The Annual Report to the Nation provides recent trends in rates of new cancer cases (incidence) and death rates (mortality) in the United States.
> - Overall, cancer death rates decreased 2.2% per year (on average) among males and 1.7% per year (on average) among females.
> - Cancer death rates decreased an average of 0.9% per year among AYAs, and an average of 1.4% per year among children between 2014 and 2018.
> - Overall cancer incidence rates are leveling off among males after earlier declines and increasing slightly among females and AYAs.
> - These trends reflect population changes in cancer risk factors (such as excess body weight), screening test use and diagnostic practices.
> - The most common cancer types among children included leukemia, brain and other nervous system, and lymphoma, with increasing incidence trends for all three from 2001-2017."
>
> Annual Report to the Nation on the Status of Cancer, Part 1: National Cancer Statistics

Peer-Reviewed Articles

BMJ: Risks of covid-19 hospital admission and death for people with learning disability: population based cohort study using the OpenSAFELY platform (14 July 2021)

> "Objective: To assess the association between learning disability and risk of hospital admission and death from covid-19 in England among adults and children.

> Setting: Patient level data were obtained for more than 17 million people registered with a general practice in England that uses TPP software. Electronic health records were linked with death data from the Office for National Statistics and hospital admission data from NHS Secondary Uses Service.
>
> Participants: Adults (aged 16-105 years) and children (<16 years) from two cohorts: wave 1 (registered with a TPP practice as of 1 March 2020 and followed until 31 August 2020); and wave 2 (registered 1 September 2020 and followed until 8 February 2021). The main exposure group consisted of people on a general practice learning disability register; a subgroup was defined as those having profound or severe learning disability. People with Down's syndrome and cerebral palsy were identified (whether or not they were on the learning disability register).
>
> Results: For wave 1, 14 312 023 adults aged ≥16 years were included, and 90 307 (0.63%) were on the learning disability register. Among adults on the register, 538 (0.6%) had a covid-19 related hospital admission; there were 222 (0.25%) covid-19 related deaths and 602 (0.7%) non-covid deaths. Among adults not on the register, 29 781 (0.2%) had a covid-19 related hospital admission; there were 13 737 (0.1%) covid-19 related deaths and 69 837 (0.5%) non-covid deaths. Wave 1 hazard ratios for adults on the learning disability register (adjusted for age, sex, ethnicity, and geographical location) were 5.3 (95% confidence interval 4.9 to 5.8) for covid-19 related hospital admission and 8.2 (7.2 to 9.4) for covid-19 related death. Wave 2 produced similar estimates. Associations were stronger among those classified as having severe to profound learning disability, and among those in residential care. For both waves, Down's syndrome and cerebral palsy were associated with increased hazards for both events; Down's syndrome to a greater extent. Hazard ratios for non-covid deaths followed similar patterns with weaker associations. Similar patterns of increased relative risk were seen for children, but covid-19 related deaths and hospital admissions were rare, reflecting low event rates among children.
>
> Conclusions: People with learning disability have markedly increased risks of hospital admission and death from covid-19, over and above the risks observed for non-covid causes of death. Prompt access to covid-19 testing and healthcare is warranted for this vulnerable group, and prioritisation for covid-19 vaccination and other targeted preventive measures should be considered."

JAMA Intern Med: Association of BNT162b2 mRNA and mRNA-1273 Vaccines With COVID-19 Infection and Hospitalization Among Patients With Cirrhosis (13 July 2021)

> "Question Are COVID-19 mRNA vaccines associated with decrease in COVID-19 infections and death in a real-world setting among patients with cirrhosis of the liver?
>
> Findings In this retrospective cohort study of US veterans with cirrhosis that compared 20 037 patients who received either a Pfizer BNT162b2 mRNA or a Moderna mRNA-1273

> COVID-19 vaccine with 20 037 propensity score matched controls, receipt of 1 dose of either vaccine was associated with a 64.8% reduction in COVID-19 infections and 100% reduction in hospitalization or death due to COVID-19 infection after 28 days.
>
> Meaning This cohort study found that mRNA vaccines against COVID-19 were associated with reduced COVID-19 infections in individuals with cirrhosis, despite hyporesponsiveness to other vaccines."

JAMA Oncol: Serologic Status and Toxic Effects of the SARS-CoV-2 BNT162b2 Vaccine in Patients Undergoing Treatment for Cancer (08 July 2021)

> "Question What is the serologic status and incidence of adverse effects in patients with cancer who are receiving therapy after administration of the SARS-CoV-2 BNT162b2 vaccine?
>
> Findings This cohort study evaluated serologic status and safety of the BNT162b2 vaccine in 232 patients receiving active treatment for cancer and 261 health care workers who served as controls. After the first dose of the vaccine, 29% of the patients were seropositive compared with 84% of the controls; after the second dose, the seropositive rate of the patients reached 86%, and reported adverse events resembled those of healthy individuals.
>
> Meaning The SARS-CoV-2 BNT162b2 vaccine appears to be safe with satisfactory levels of seropositivity in patients undergoing treatment for cancer, although protection may occur later compared with the healthy population."

JAMA: Changes in Patterns of Hospital Visits for Acute Myocardial Infarction or Ischemic Stroke During COVID-19 Surges (02 July 2021)

> "This study evaluates changes in rates of patients hospitalized for acute myocardial infarction (AMI) or suspected stroke during COVID-19 surges in the US as a measure of willingness to seek care during the pandemic….
>
> In contrast to the initial COVID-19 surge during March to April 2020 in the US and to recent data from the UK, no significant declines in AMI hospitalization or stroke alerts were observed during the largest and most recent surge during October 2020 to January 2021/"

JAMA Intern Med: Diabetes Care and Glycemic Control During the COVID-19 Pandemic in the United States (06 July 2021)

> "This cohort study compares rates at which patients with type 2 diabetes received diabetes-related health services prior to and during the COVID-19 pandemic….
>
> While diabetes-related outpatient visits and testing fell during the pandemic, we observed no evidence of a negative association with medication fills or glycemic control."

Long COVID / Post-COVID Period

News in Brief

"Long COVID and kids: scientists race to find answers: Children get long COVID too, but researchers are still working to determine how frequently and how severely" (Nature; see also: Acta Paediatrica article detailed below in Pediatric Population section).

"Are latent viruses causing long Covid-19 symptoms? Patient groups push for testing: A new theory that reactivated older viruses are driving some of the coronavirus's debilitating symptoms is gaining traction among some patient advocates" (WSJ).

Peer-Reviewed Articles

EClinicalMedicine: Characterizing long COVID in an international cohort: 7 months of symptoms and their impact (15 July 2021)

> "Background A significant number of patients with COVID-19 experience prolonged symptoms, known as Long COVID. Few systematic studies have investigated this population, particularly in outpatient settings. Hence, relatively little is known about symptom makeup and severity, expected clinical course, impact on daily functioning, and return to baseline health.
>
> Methods We conducted an online survey of people with suspected and confirmed COVID-19, distributed via COVID-19 support groups (e.g. Body Politic, Long COVID Support Group, Long Haul COVID Fighters) and social media (e.g. Twitter, Facebook). Data were collected from September 6, 2020 to November 25, 2020. We analyzed responses from 3762 participants with confirmed (diagnostic/antibody positive; 1020) or suspected (diagnostic/antibody negative or untested; 2742) COVID-19, from 56 countries, with illness lasting over 28 days and onset prior to June 2020. We estimated the prevalence of 203 symptoms in 10 organ systems and traced 66 symptoms over seven months. We measured the impact on life, work, and return to baseline health.
>
> Findings For the majority of respondents (>91%), the time to recovery exceeded 35 weeks. During their illness, participants experienced an average of 55.9+/- 25.5 (mean+/-STD) symptoms, across an average of 9.1 organ systems. The most frequent symptoms after month 6 were fatigue, post-exertional malaise, and cognitive dysfunction. Symptoms varied in their prevalence over time, and we identified three symptom clusters, each with a characteristic temporal profile. 85.9% of participants (95% CI, 84.8% to 87.0%) experienced relapses, primarily triggered by exercise, physical or mental activity, and stress. 86.7% (85.6% to 92.5%) of unrecovered respondents were experiencing fatigue at the time of survey, compared to 44.7% (38.5% to 50.5%) of recovered respondents. 1700 respondents

> (45.2%) required a reduced work schedule compared to pre-illness, and an additional 839 (22.3%) were not working at the time of survey due to illness. Cognitive dysfunction or memory issues were common across all age groups (~88%). Except for loss of smell and taste, the prevalence and trajectory of all symptoms were similar between groups with confirmed and suspected COVID-19.
>
> Interpretation Patients with Long COVID report prolonged, multisystem involvement and significant disability. By seven months, many patients have not yet recovered (mainly from systemic and neurological/cognitive symptoms), have not returned to previous levels of work, and continue to experience significant symptom burden."

MMWR: Outcomes Among Patients Referred to Outpatient Rehabilitation Clinics After COVID-19 diagnosis — United States, January 2020–March 2021 (09 July 2021)

> "What is already known about this topic? COVID-19 patients might experience symptoms that persist months after initial infection.
>
> What is added by this report? Compared with control patients enrolled in a cancer rehabilitation program, adult post–COVID-19 patients referred for rehabilitation services reported poorer physical health and being less able to engage in physical activities and activities of daily living. Patients recovering from COVID-19 also had significantly higher health care use than control patients.
>
> What are the implications for public health practice? Patients recovering from COVID-19 might require tailored physical and mental health rehabilitation services."

J Am Board Fam Med: Risk of New Hospitalization Post COVID-19 Infection for Non-COVID-19 Conditions (accessed 15 July 2021)

> "Introduction: Reports of post-acute sequelae of COVID-19 continue to emerge, but it remains unclear how the severity of a patient’s COVID-19 infection affects risk for future hospitalizations for non-COVID-19 problems.
>
> Methods: An analysis of electronic health records (EHR) was performed for a cohort of 10,646 patients who were followed for 6 months post COVID-19 episode at one health system. COVID-19 positive patients were classified as severe if they were hospitalized within the first 30 days of their initial positive test. Assessment of hospitalizations overall and for conditions that could be seen as complications of COVID-19 (cardiovascular, respiratory, and clotting diagnoses) were assessed. The 6-month risk of a new hospitalization was assessed in both unadjusted and adjusted Cox regressions.
>
> Results: Of the 10,646 patients included in this cohort,114 had severe COVID-19, 211 had mild/moderate COVID-19, and 10,321 were COVID-19 negative. After adjustment for potential confounding variables, there was no significantly increased risk in future

> hospitalization for any condition for patients who were COVID-19 positive versus those who were COVID-19 negative (HR 1.31; 95% CI 0.98, 1.74). In adjusted analyses, individuals with severe COVID-19 had an increased risk of hospitalization for potential complications compared to both mild/moderate COVID-19 (HR 2.20; 95% CI 1.13, 4.28) and COVID-19 negative patients (HR 2.24; 95% CI: 1.52, 3.30).
>
> Discussion: Patients with a severe COVID-19 episode were at greater risk for future hospitalizations. This study reinforces the importance of preventing infection in patients at higher risk for severe COVID-19 cases."

JAMA Netw Open: Assessment of Prolonged Physiological and Behavioral Changes Associated With COVID-19 Infection (07 July 2021)

> "This cohort study examines the duration and variation of recovery among COVID-19–positive verses COVID-19–negative individuals….
>
> To our knowledge, this is the first study to examine longer duration wearable sensor data. We found a prolonged physiological impact of COVID-19 infection, lasting approximately 2 to 3 months, on average, but with substantial intraindividual variability, which may reflect various levels of autonomic nervous system dysfunction or potentially ongoing inflammation. Transient bradycardia has been noted in a case study approximately 9 to 15 days after symptom onset, which was also seen in our population. Our data suggest that early symptoms and larger initial RHR response to COVID-19 infection may be associated with the physiological length of recovery from this virus."

Ann Intern Med: Prevalence of Symptoms More Than Seven Months After Diagnosis of Symptomatic COVID-19 in an Outpatient Setting (06 July 2021)

> "Background: With millions of SARS-CoV-2 infections worldwide, increasing numbers of patients are coming forward with long-term clinical effects of the disease lasting several weeks to months.
>
> Objective: To characterize symptoms 7 to 9 months after diagnosis of COVID-19.
>
> Design: Self-reported surveys and semistructured telephone interviews at enrollment and 30 to 45 days and 7 to 9 months from diagnosis.
>
> Setting: From 18 March to 15 May 2020, symptomatic persons who tested positive for SARS-CoV-2 at the Geneva University Hospitals were followed by CoviCare, a virtual, clinical, outpatient follow-up program. Persons were contacted again at 30 to 45 days and 7 to 9 months from diagnosis.
>
> Participants: Persons who were a part of the CoviCare program from 18 March to 15 May 2020.

> Measurements: A standardized interview of symptoms consistent with COVID-19, with grading of intensity.
>
> Results: Of the 629 participants in the study who completed the baseline interviews, 410 completed follow-up at 7 to 9 months after COVID-19 diagnosis; 39.0% reported residual symptoms. Fatigue (20.7%) was the most common symptom reported, followed by loss of taste or smell (16.8%), dyspnea (11.7%), and headache (10.0%).
>
> Limitation: Limitations include generalizability and missing data for 34.8% of participants.
>
> Conclusion: Residual symptoms after SARS-CoV-2 infection are common among otherwise young and healthy persons followed in an outpatient setting. These findings contribute to the recognition of long-term effects in a disease mostly counted by its death toll to date by promoting communication on postacute sequelae of SARS-CoV-2 and encouraging physicians to continue long-term monitoring of their patients."

Clin Infect Dis: Persistent symptoms in adult patients one year after COVID-19: a prospective cohort study (05 July 2021)

> "Background: Long COVID is defined as the persistence of symptoms beyond 3 months after SARS-CoV-2 infection. To better understand the long-term course and etiology of symptoms we analyzed a cohort of COVID-19 patients prospectively.
>
> Methods: Patients were included at 5 months after acute COVID-19 in this prospective, non-interventional follow-up study. Patients followed until 12 months after COVID-19 symptom onset (n=96, 32.3% hospitalised, 55.2% females) were included in this analysis of symptoms, quality of life (based on a SF-12 survey), laboratory parameters including antinuclear antibodies (ANA), and SARS-CoV-2 antibody levels.
>
> Results: At month 12, only 22.9% of patients were completely free of symptoms and the most frequent symptoms were reduced exercise capacity (56.3%), fatigue (53.1%), dyspnoea (37.5%), concentration problems (39.6%), problems finding words (32.3%), and sleeping problems (26.0%). Females showed significantly more neurocognitive symptoms than males.ANA titres were ≥1:160 in 43.6% of patients at 12 months post COVID-19 symptom onset, and neurocognitive symptom frequency was significantly higher in the group with an ANA titre ≥1:160 compared to <1:160. Compared to patients without symptoms, patients with at least one long COVID symptom at 12 months did not differ significantly with respect to their SARS-CoV-2-antibody levels, but had a significantly reduced physical and mental life quality compared to patients without symptoms.
>
> Conclusions: Neurocognitive long COVID symptoms can persist at least for one year after COVID-19 symptom onset, and reduce life quality significantly. Several neurocognitive symptoms were associated with ANA titre elevations. This may indicate autoimmunity as cofactor in aetiology of long COVID."

Women's Health, Pregnancy, and Perinatal Care

Peer-Reviewed Articles

JAMA Netw Open: Association Between BNT162b2 Vaccination and Incidence of SARS-CoV-2 Infection in Pregnant Women (12 July 2021)

> "Question Among pregnant women, what is the association between receipt of BNT162b2 messenger RNA vaccine and risk of SARS-CoV-2 infection?
>
> Findings In a retrospective cohort study that included 15 060 pregnant women in Israel, vaccination with BNT162b2 vs nonvaccination was associated with an adjusted hazard ratio for incident SARS-CoV-2 infection of 0.22; this was statistically significant.
>
> Meaning Among pregnant women, receipt of the BNT162b2 vaccine was associated with a lower risk of incident SARS-CoV-2 infection."

JAMA Pediatr: Evaluation of Messenger RNA From COVID-19 BTN162b2 and mRNA-1273 Vaccines in Human Milk (06 July 2021)

> "This cohort study analyzes milk samples from lactating mothers to determine if COVID-19 vaccine–related messenger RNA was detectable in human milk after vaccination….
>
> Vaccine-associated mRNA was not detected in 13 milk samples collected 4 to 48 hours after vaccination from 7 breastfeeding individuals. These results provide important early evidence to strengthen current recommendations that vaccine-related mRNA is not transferred to the infant and that lactating individuals who receive the COVID-19 mRNA-based vaccine should not stop breastfeeding. In addition, any residual mRNA below the limits of detection in our assay would undergo degradation by the infant gastrointestinal system, further reducing infant exposure."

Pediatric Population

News in Brief

COVID-19 pandemic leads to major backsliding on childhood vaccinations, new WHO, UNICEF data shows" (WHO; see also Lancet article detailed below).

"The effects of COVID-19 on kids are even stranger than we thought: Doctors have found a concerning link between the rare pediatric complication known as MIS-C and a syndrome related to tampon use" (Atlantic).

"Will COVID become a disease of the young? A growing share of infections among unvaccinated youths in countries with high vaccination rates is putting the spotlight on the role of young people in the pandemic" (Nature; see also: Coronapod podcast).

"Deaths from COVID 'incredibly rare' among children: Studies find that overall risk of death or severe disease from COVID-19 is very low in kids" (Nature; includes links to preprints).

Photos: "With 4 million COVID dead, many kids left behind" (AP).

Peer-Reviewed Articles

JAMA: Long-term Symptoms After SARS-CoV-2 Infection in Children and Adolescents (15 July 2021)

> "This cohort study reports the prevalence of long-term symptoms in children and adolescents who had recovered from acute SARS-CoV-2 infection….
>
> This study found a low prevalence of symptoms compatible with long COVID in a randomly selected cohort of children assessed 6 months after serologic testing.
>
> Although long COVID exists in children, estimates of the prevalence of persisting symptoms based on scarce literature range from 0%2 to 27%. Initial SARS-CoV-2 infection severity, different methodological approaches (clinical assessment vs self-report), definition of cases (diagnosed vs suspected), variable follow-up times, and prevalence of preexisting clinical conditions likely contribute to the variability in prevalence estimates.
>
> This study reports the distribution of symptoms compatible with long COVID on a population level; it did not capture severe SARS-CoV-2 infections because they are rare in children."

Lancet: Estimating global and regional disruptions to routine childhood vaccine coverage during the COVID-19 pandemic in 2020: a modelling study (14 July 2021)

> "Background The COVID-19 pandemic and efforts to reduce SARS-CoV-2 transmission substantially affected health services worldwide. To better understand the impact of the pandemic on childhood routine immunisation, we estimated disruptions in vaccine coverage associated with the pandemic in 2020, globally and by Global Burden of Disease (GBD) super-region.
>
> Methods For this analysis we used a two-step hierarchical random spline modelling approach to estimate global and regional disruptions to routine immunisation using administrative data and reports from electronic immunisation systems, with mobility data as a model input. Paired with estimates of vaccine coverage expected in the absence of COVID-19, which were derived from vaccine coverage models from GBD 2020, Release 1

> (GBD 2020 R1), we estimated the number of children who missed routinely delivered doses of the third-dose diphtheria-tetanus-pertussis (DTP3) vaccine and first-dose measles-containing vaccine (MCV1) in 2020.
>
> Findings Globally, in 2020, estimated vaccine coverage was 76·7% (95% uncertainty interval 74·3–78·6) for DTP3 and 78·9% (74·8–81·9) for MCV1, representing relative reductions of 7·7% (6·0–10·1) for DTP3 and 7·9% (5·2–11·7) for MCV1, compared to expected doses delivered in the absence of the COVID-19 pandemic. From January to December, 2020, we estimated that 30·0 million (27·6–33·1) children missed doses of DTP3 and 27·2 million (23·4–32·5) children missed MCV1 doses. Compared to expected gaps in coverage for eligible children in 2020, these estimates represented an additional 8·5 million (6·5–11·6) children not routinely vaccinated with DTP3 and an additional 8·9 million (5·7–13·7) children not routinely vaccinated with MCV1 attributable to the COVID-19 pandemic. Globally, monthly disruptions were highest in April, 2020, across all GBD super-regions, with 4·6 million (4·0–5·4) children missing doses of DTP3 and 4·4 million (3·7–5·2) children missing doses of MCV1. Every GBD super-region saw reductions in vaccine coverage in March and April, with the most severe annual impacts in north Africa and the Middle East, south Asia, and Latin America and the Caribbean. We estimated the lowest annual reductions in vaccine delivery in sub-Saharan Africa, where disruptions remained minimal throughout the year. For some super-regions, including southeast Asia, east Asia, and Oceania for both DTP3 and MCV1, the high-income super-region for DTP3, and south Asia for MCV1, estimates suggest that monthly doses were delivered at or above expected levels during the second half of 2020.
>
> Interpretation Routine immunisation services faced stark challenges in 2020, with the COVID-19 pandemic causing the most widespread and largest global disruption in recent history. Although the latest coverage trajectories point towards recovery in some regions, a combination of lagging catch-up immunisation services, continued SARS-CoV-2 transmission, and persistent gaps in vaccine coverage before the pandemic still left millions of children under-vaccinated or unvaccinated against preventable diseases at the end of 2020, and these gaps are likely to extend throughout 2021. Strengthening routine immunisation data systems and efforts to target resources and outreach will be essential to minimise the risk of vaccine-preventable disease outbreaks, reach children who missed routine vaccine doses during the pandemic, and accelerate progress towards higher and more equitable vaccination coverage over the next decade."

JAMA Netw Open: Prevalence of Serious Bacterial Infections Among Febrile Infants 90 Days or Younger in a Canadian Urban Pediatric Emergency Department During the COVID-19 Pandemic (13 July 2021)

> "This cross-sectional study compares the prevalence of severe bacterial infections [SBIs] in febrile neonates and infants before vs during the COVID-19 pandemic in Montreal, Quebec, Canada….
>
> During the COVID-19 pandemic, ED visits among febrile young infants decreased 66.3%; however, among those brought to the ED, the prevalence of SBIs doubled and the prevalence of IBIs [invasive bacterial infections] tripled. To our knowledge, this is the largest analysis of febrile young infants during the COVID-19 pandemic and the first to identify an increase in SBI prevalence during this period. These findings suggest that a high degree of caution is necessary when evaluating febrile young infants while COVID-19 public health strategies continue to be implemented."

Pediatrics: Medical Admissions Among Adolescents With Eating Disorders During the COVID-19 Pandemic (08 July 2021)

> "Background and Objectives: Emerging data suggest the COVID-19 pandemic has been associated with worsening symptoms of eating disorders among both adults and adolescents. This study sought to determine whether medical admission patterns among adolescents admitted to our institution for restrictive eating disorders changed during the pandemic, relative to prepandemic counts of admissions per month.
>
> Methods: We performed a chart review of patients ages 10-23 admitted to our children's hospital for restrictive eating disorders from March 2017 through March 2021 and completed an interrupted time series analysis of admission counts per month. Demographic variables for admitted patients were compared using $\chi 2$, Fisher's Exact, and two-sample t-tests.
>
> Results: Eating disorder-related medical admissions at our institution increased significantly during the COVID-19 pandemic. The total number of admissions during the first twelve months of the COVID-19 pandemic (April 1, 2020 through March 31, 2021, n = 125) was more than double the mean number of admissions per year for the same time frame (April 1 through March 31) for the previous three years (mean = 56). Patient demographics were similar before and during the pandemic, with the exception that patients admitted during the COVID-19 pandemic were less likely than those admitted prior to the pandemic to have public insurance.
>
> Conclusions: Medical admissions related to restrictive eating disorders among adolescents increased significantly during the COVID-19 pandemic. Pediatric providers in a variety of settings should be prepared to care for adolescents with restrictive eating disorders during the pandemic."

Circulation: Diagnosis and Management of Myocarditis in Children: A Scientific Statement From the American Heart Association (07 July 2021)

> "Myocarditis remains a clinical challenge in pediatrics. Originally, it was recognized at autopsy before the application of endomyocardial biopsy, which led to a histopathology-based diagnosis such as in the Dallas criteria. Given the invasive and low-sensitivity nature of endomyocardial biopsy, its diagnostic focus shifted to a reliance on clinical suspicion. With the advances of cardiac magnetic resonance, an examination of the whole heart in vivo has gained acceptance in the pursuit of a diagnosis of myocarditis. The presentation may vary from minimal symptoms to heart failure, life-threatening arrhythmias, or cardiogenic shock. Outcomes span full resolution to chronic heart failure and the need for heart transplantation with inadequate clues to predict the disease trajectory. The American Heart Association commissioned this writing group to explore the current knowledge and management within the field of pediatric myocarditis. This statement highlights advances in our understanding of the immunopathogenesis, new and shifting dominant pathogeneses, modern laboratory testing, and use of mechanical circulatory support, with a special emphasis on innovations in cardiac magnetic resonance imaging. Despite these strides forward, we struggle without a universally accepted definition of myocarditis, which impedes progress in disease-targeted therapy."

Pediatrics: Collaborating to Advocate in Primary Care for Children During COVID-19 (07 July 2021)

> "The St. Louis Regional Pediatric Learning Collaborative of pediatric primary care providers (PCPs) and infectious diseases specialists formed in March 2020 to address the needs of children and families during the Coronavirus Disease-2019 (COVID-19) pandemic. Over 400 PCPs participated using a listserv to discuss care and organize webinars to provide updates on local and national data and plan next steps. To inform local decision making about care and testing for SARS-CoV-2, 95 providers from 26 practices partnered with the local practice-based research network to rapidly collect and share data about children with COVID-19-like symptoms. Of 2162 children tested for SARS-CoV-2, 9% tested positive. Test positivity was 33% if a patient was exposed to a confirmed case of COVID-19 and 4% if they had COVID-19-like symptoms and no exposure. School/daycare attendance was associated with lower rates of positive test results. Although not originally planned, these findings drove local advocacy efforts by the Collaborative for increased access to testing and contact tracing and safe in-person school. Members communicated directly and collectively with local politicians, provided advice and resources for school boards and superintendent groups, and appeared on various media platforms. In these efforts they shared local data, highlighting the lower rate of positive tests for children in school to support the idea that schools could be safely open. Outreach from trusted pediatricians sharing prospective,

> timely, local data sustained in-person school for some districts and aided in future in-person openings for other school districts."

JAMA Pediatr: Disparities in Susceptibility to Multisystem Inflammatory Syndrome in Children (06 July 2021)

> "This Viewpoint discusses what factors have led to the disproportionate effects multisystem inflammatory syndrome has had on Black and Hispanic children."

Acta Paediatr: Preliminary evidence on long COVID in children (09 April 2021)

> "This is a large series study providing evidence of Long COVID in children, and currently to our knowledge in literature, there is another report supporting the topic. More than a half of the children assessed during the survey reported at least one symptom. In particular, 42.6% presented at least one symptoms >60 days after infection. Symptoms like fatigue, muscle and joint pain, headache, insomnia, respiratory problems and palpitations were particularly frequent, as also described in adults. To date, the only other paediatric study available is a Swedish case series of five children, all suffering from fatigue, dyspnoea, heart palpitations or chest pain after >60 days from initial diagnosis. Importantly, all those Swedish children had persistent symptoms after 6 months. These findings are in line with the patterns of symptoms reported in our cohort. Also, the Swedish children with Long COVID had a median age of 12 years, similar to our children (11.4 years), further supporting that this age group may particularly suffer from Long COVID."

Impact on Healthcare Workers

News in Brief

Long read: "Their neighbors called covid-19 a hoax. Can these ICU nurses forgive them? For the nurses in the Appalachian highlands who risked their lives during the pandemic, it is as if they fought in a war no one acknowledges" (WP).

"Carolina Stress Initiative recruiting health care workers for study to develop better mental health therapies" (WRAL).

Peer-Reviewed Articles

Clin Infect Dis: An observational cohort study on the incidence of SARS-CoV-2 infection and B.1.1.7 variant infection in healthcare workers by antibody and vaccination status (03 July 2021)

> "Background: Natural and vaccine-induced immunity will play a key role in controlling the SARS-CoV-2 pandemic. SARS-CoV-2 variants have the potential to evade natural and vaccine-induced immunity.
>
> Methods: In a longitudinal cohort study of healthcare workers (HCWs) in Oxfordshire, UK, we investigated the protection from symptomatic and asymptomatic PCR-confirmed SARS-CoV-2 infection conferred by vaccination (Pfizer-BioNTech BNT162b2, Oxford-AstraZeneca ChAdOx1 nCOV-19) and prior infection (determined using anti-spike antibody status), using Poisson regression adjusted for age, sex, temporal changes in incidence and role. We estimated protection conferred after one versus two vaccinations and from infections with the B.1.1.7 variant identified using whole genome sequencing.
>
> Results: 13,109 HCWs participated; 8285 received the Pfizer-BioNTech vaccine (1407 two doses) and 2738 the Oxford-AstraZeneca vaccine (49 two doses). Compared to unvaccinated seronegative HCWs, natural immunity and two vaccination doses provided similar protection against symptomatic infection: no HCW vaccinated twice had symptomatic infection, and incidence was 98% lower in seropositive HCWs (adjusted incidence rate ratio 0.02 [95%CI <0.01-0.18]). Two vaccine doses or seropositivity reduced the incidence of any PCR-positive result with or without symptoms by 90% (0.10 [0.02-0.38]) and 85% (0.15 [0.08-0.26]) respectively. Single-dose vaccination reduced the incidence of symptomatic infection by 67% (0.33 [0.21-0.52]) and any PCR-positive result by 64% (0.36 [0.26-0.50]). There was no evidence of differences in immunity induced by natural infection and vaccination for infections with S-gene target failure and B.1.1.7.
>
> Conclusion: Natural infection resulting in detectable anti-spike antibodies and two vaccine doses both provide robust protection against SARS-CoV-2 infection, including against the B.1.1.7 variant."

Emerg Infect Dis: Risk for Acquiring COVID-19 Illness among Emergency Medical Service Personnel Exposed to Aerosol-Generating Procedures (01 July 2021)

> "We investigated the risk of coronavirus disease (COVID-19)- patients transmitting severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) to emergency medical service (EMS) providers, stratified by aerosol-generating procedures (AGP), in King County, Washington, USA, during February 16–July 31, 2020. We conducted a retrospective cohort investigation using a statewide COVID-19 registry and identified 1,115 encounters, 182 with ≥1 AGP. Overall, COVID-19 incidence among EMS personnel was 0.57 infections/10,000 person-days. Incidence per 10,000 person-days did not differ whether or not infection was attributed to a COVID-19 patient encounter (0.28 vs. 0.59; p>0.05). The 1 case attributed to a COVID-19 patient encounter occurred within an at-risk period and involved an AGP. We observed a very low risk for COVID-19 infection attributable to patient encounters among

> EMS first responders, supporting clinical strategies that maintain established practices for treating patients in emergency conditions."

PLoS One: Dilemma of physician-mothers faced with an increased home burden and clinical duties in the hospital during the COVID-19 pandemic (24 June 2021)

> "Purpose: Since December 2019, coronavirus disease 2019 (COVID-19) has spread rapidly across the world. During the pandemic, physicians in our hospital have had to respond both to the issue of treating the patients and the increasing domestic burden associated with social disruption. The purpose of this study was to assess how much the burden on our doctors, especially female doctors, was increasing.
>
> Material and methods: The Physicians' Career Support Committee in Sapporo Medical University conducted a questionnaire survey. The questionnaire inquired about a wide range of subjects with regard to working style and family life during the first and second waves of the COVID-19 pandemic, and was sent to all medical/dental physicians working in Sapporo Medical University.
>
> Results: A total of 266 (42.7%) physicians in our hospital responded to our questionnaire and the data for 264 data were analyzed. The total numbers of males, females, and others, including those who did not want to specify, were 178 (67.4%), 82 (31.0%), and 4 (1.5%), respectively. Among them, 62 (23.5%) and 23 (8.7%) answered that their domestic burden was slightly or markedly increased. The increase in the domestic burden showed a significant difference between genders ($p = 0.04$). Even after correction for background differences using multivariate analysis, being female ($p<0.001$), having child dependents ($p<0.001$), and treating COVID-19 patients ($p = 0.03$) were significantly related to an increased domestic burden. Regarding family style, 58.1% of the physician-fathers were from two-income families (i.e., families with both parents in employment), and they answered that their partner mainly cared for the children. In contrast, 97.3% of physician-mothers were from two-income families, and 94.6% of the physician-mothers had to take care of children by themselves.
>
> Conclusion: Physician-mothers are caught in a dilemma between an increased home burden and clinical duties in the hospital, with a significantly higher ratio than physician-fathers during the pandemic. As we showed, female doctors could have not continued their careers and take responsible positions in the same way as male doctors. This is a social risk in the timing of a crisis, such as a pandemic."

Mental Health, Psychosocial Issues, and Wellness

News in Brief

CVS has a program offering mental health counseling in its MinuteClinic; the service is available in 4 states: Florida, New Jersey, Pennsylvania, and Texas, with plans to expand (CVS).

Peer-Reviewed Articles

PLoS One: Evaluating the association between COVID-19 and psychiatric presentations, suicidal ideation in an emergency department (30 June 2021)

> "Objective: To estimate the association between COVID-19 and Emergency Department (ED) psychiatric presentations, including suicidal ideation.
>
> Methods: Using an interrupted time series design, we analyzed psychiatric presentations using electronic health record data in an academic medical center ED between 2018 and 2020. We used regression models to assess the association between the onset of the COVID-19 outbreak and certain psychiatric presentations. The period February 26-March 6, 2020 was used to define patterns in psychiatric presentations before and after the coronavirus outbreak.
>
> Results: We found a 36.2% decrease (unadjusted) in ED psychiatric consults following the coronavirus outbreak, as compared to the previous year. After accounting for underlying trends, our results estimate significant differential change associated with suicidal ideation and substance use disorder (SUD) presentations following the outbreak. Specifically, we noted a significant differential increase in presentations with suicidal ideation six weeks after the outbreak (36.4 percentage points change; 95% CI: 5.3, 67.6). For presentations with SUD, we found a differential increase in the COVID-19 time series relative to the comparison time series at all post-outbreak time points and this differential increase was significant three weeks (32.8 percentage points; 95% CI: 4.0, 61.6) following the outbreak. Our results estimate no differential changes significant at the P value < 0.05 level associated with affective disorder or psychotic disorder presentations in the COVID-19 time series relative to the comparator time series.
>
> Conclusions: The COVID-19 outbreak in Boston was associated with significant differential increases in ED presentations with suicidal ideation and SUD."

Disparities and Health Equity

News in Brief

"COVID-19 affects men and women differently. So why don’t clinical trials report gender data?" (Science).

Peer-Reviewed Articles

JAMA Netw Open: Effect of Physician-Delivered COVID-19 Public Health Messages and Messages Acknowledging Racial Inequity on Black and White Adults' Knowledge, Beliefs, and Practices Related to COVID-19: A Randomized Clinical Trial (14 July 2021)

> "Question Do messages delivered by physicians increase COVID-19 knowledge and improve preventive behaviors among White and Black individuals?
>
> Findings In this randomized clinical trial of 18 223 White and Black adults, a message delivered by a physician increased COVID-19 knowledge and shifted information-seeking and self-protective behaviors. Effects did not differ by race, and tailoring messages to specific communities did not exhibit a differential effect on knowledge or individual behavior.
>
> Meaning These findings suggest that physician messaging campaigns may be effective in persuading members of society from a broad range of backgrounds to seek information and adopt preventive behaviors to combat COVID-19."

Nat Commun: Lack of consideration of sex and gender in COVID-19 clinical studies (06 July 2021)

> "Sex and gender differences impact the incidence of SARS-CoV-2 infection and COVID-19 mortality. Furthermore, sex differences influence the frequency and severity of pharmacological side effects. A large number of clinical trials to develop new therapeutic approaches and vaccines for COVID-19 are ongoing. We investigated the inclusion of sex and/or gender in COVID-19 studies on ClinicalTrials.gov, collecting data for the period January 1, 2020 to January 26, 2021. Here, we show that of the 4,420 registered SARS-CoV-2/COVID-19 studies, 935 (21.2%) address sex/gender solely in the context of recruitment, 237 (5.4%) plan sex-matched or representative samples or emphasized sex/gender reporting, and only 178 (4%) explicitly report a plan to include sex/gender as an analytical variable. Just eight (17.8%) of the 45 COVID-19 related clinical trials published in scientific journals until December 15, 2020 report sex-disaggregated results or subgroup analyses."

JAMA Netw Open: Evaluation of Health Equity in COVID-19 Vaccine Distribution Plans in the United States (02 July 2021)

> "This cross-sectional study evaluates measures of health equity in COVID-19 vaccination plans in the 50 US states and Washington, DC….
>
> In this cross-sectional study, most COVID-19 vaccination plans were created without advisement from a health equity committee. This is concerning because there is a disproportionate burden of severe COVID-19 disease and mortality among racial and ethnic minority groups."

Risk, Transmission, and Exposure

News in Brief

"No fast music or fast running: COVID rules in Seoul force gym-goers to slow down" (NPR).

"Two new unpublished studies suggest that people who have COVID-19 often spread it to their dogs and cats—particularly if they share a bed with their cats—although the pets usually have no or mild symptoms but in a few cases might have severe disease." Pet to human transmission has not been reported (CIDRAP; see also: ECCMID news release).

Peer-Reviewed Articles

MMWR: SARS-CoV-2 B.1.617.2 (Delta) Variant COVID-19 Outbreak Associated with a Gymnastics Facility — Oklahoma, April–May 2021 (09 July 2021)

> "What is already known about this topic? The SARS-CoV-2 B.1.617.2 (Delta) variant emerged in India and is currently widespread. Evidence suggests that it is potentially more transmissible than other variants.
>
> What is added by this report? During April 15–May 3, 2021, 47 COVID-19 cases were linked to a gymnastics facility, including 21 laboratory-confirmed B.1.617.2 cases and 26 epidemiologically linked cases. The overall facility and household attack rates were 20% and 53%, respectively.
>
> What are the implications for public health practice? The B.1.617.2 variant is highly transmissible in indoor sports settings and households, which might lead to increased attack rates. Multicomponent prevention strategies including vaccination remain important to reduce the spread of SARS-CoV-2 among persons participating in indoor sports and their contacts."

MMWR: Efficacy of Portable Air Cleaners and Masking for Reducing Indoor Exposure to Simulated Exhaled SARS-CoV-2 Aerosols — United States, 2021 (09 July 2021)

> "What is already known about this topic? Ventilation systems can be supplemented with portable high efficiency particulate air (HEPA) cleaners to reduce the number of airborne infectious particles.
>
> What is added by this report? A simulated infected meeting participant who was exhaling aerosols was placed in a room with two simulated uninfected participants and a simulated uninfected speaker. Using two HEPA air cleaners close to the aerosol source reduced the aerosol exposure of the uninfected participants and speaker by up to 65%. A combination of HEPA air cleaners and universal masking reduced exposure by up to 90%.
>
> What are the implications for public health practice? Portable HEPA air cleaners can reduce exposure to simulated SARS-CoV-2 aerosols in indoor environments, especially when combined with universal masking."

Testing and Serosurveillance

Peer-Reviewed Articles

JAMA Otolaryngol Head Neck Surg: A Rapid Olfactory Test as a Potential Screening Tool for COVID-19 (15 July 2021)

> "This prospective study assesses the feasibility of a novel, objective olfactory test as part of an initial screening of COVID-19 in adults with unknown disease status….
>
> In this study, we demonstrate that a rapid psychophysical olfaction test is feasible as a screening tool for COVID-19. Current literature suggests that individuals may fail to recognize OD that is detectable on objective testing. Furthermore, screening questionnaires may miss more than 50% of COVID-19 cases, owing to screening question variation, subjective interpretation of symptom severity, and intentional patient evasion. Meanwhile, antigen-based point-of-care screening remains time intensive, expensive, and unrealistic in certain environments."

Lancet Microbe: Blood transcriptional biomarkers of acute viral infection for detection of pre-symptomatic SARS-CoV-2 infection: a nested, case-control diagnostic accuracy study (06 July 2021)

> "Background: We hypothesised that host-response biomarkers of viral infections might contribute to early identification of individuals infected with SARS-CoV-2, which is critical to breaking the chains of transmission. We aimed to evaluate the diagnostic accuracy of existing candidate whole-blood transcriptomic signatures for viral infection to predict positivity of nasopharyngeal SARS-CoV-2 PCR testing.

Methods: We did a nested case-control diagnostic accuracy study among a prospective cohort of health-care workers (aged ≥18 years) at St Bartholomew's Hospital (London, UK) undergoing weekly blood and nasopharyngeal swab sampling for whole-blood RNA sequencing and SARS-CoV-2 PCR testing, when fit to attend work. We identified candidate blood transcriptomic signatures for viral infection through a systematic literature search. We searched MEDLINE for articles published between database inception and Oct 12, 2020, using comprehensive MeSH and keyword terms for "viral infection", "transcriptome", "biomarker", and "blood". We reconstructed signature scores in blood RNA sequencing data and evaluated their diagnostic accuracy for contemporaneous SARS-CoV-2 infection, compared with the gold standard of SARS-CoV-2 PCR testing, by quantifying the area under the receiver operating characteristic curve (AUROC), sensitivities, and specificities at a standardised Z score of at least 2 based on the distribution of signature scores in test-negative controls. We used pairwise DeLong tests compared with the most discriminating signature to identify the subset of best performing biomarkers. We evaluated associations between signature expression, viral load (using PCR cycle thresholds), and symptom status visually and using Spearman rank correlation. The primary outcome was the AUROC for discriminating between samples from participants who tested negative throughout the study (test-negative controls) and samples from participants with PCR-confirmed SARS-CoV-2 infection (test-positive participants) during their first week of PCR positivity.

Findings: We identified 20 candidate blood transcriptomic signatures of viral infection from 18 studies and evaluated their accuracy among 169 blood RNA samples from 96 participants over 24 weeks. Participants were recruited between March 23 and March 31, 2020. 114 samples were from 41 participants with SARS-CoV-2 infection, and 55 samples were from 55 test-negative controls. The median age of participants was 36 years (IQR 27-47) and 69 (72%) of 96 were women. Signatures had little overlap of component genes, but were mostly correlated as components of type I interferon responses. A single blood transcript for IFI27 provided the highest accuracy for discriminating between test-negative controls and test-positive individuals at the time of their first positive SARS-CoV-2 PCR result, with AUROC of 0·95 (95% CI 0·91-0·99), sensitivity 0·84 (0·70-0·93), and specificity 0·95 (0·85-0·98) at a predefined threshold (Z score >2). The transcript performed equally well in individuals with and without symptoms. Three other candidate signatures (including two to 48 transcripts) had statistically equivalent discrimination to IFI27 (AUROCs 0·91-0·95).

Interpretation: Our findings support further urgent evaluation and development of blood IFI27 transcripts as a biomarker for early phase SARS-CoV-2 infection for screening individuals at high risk of infection, such as contacts of index cases, to facilitate early case isolation and early use of antiviral treatments as they emerge."

Breakthrough Infections, Reinfections, and Coinfections

News in Brief

"Post-vaccination infections come in 2 different flavors: Lumping all breakthroughs together, regardless of symptoms, miscasts what our COVID-19 vaccines can do" (Atlantic).

Peer-Reviewed Articles

PLoS One: Bacterial superinfection in adults with COVID-19 hospitalized in two clinics in Medellín-Colombia, 2020 (13 July 2021)

> "COVID-19 represents high morbidity and mortality, its complications and lethality have increased due to bacterial superinfections. We aimed to determine the prevalence of bacterial superinfection in adults with COVID-19, hospitalized in two clinics in Medellín-Colombia during 2020, and its distribution according to sociodemographic and clinical conditions.
>
> A cross sectional study was made with 399 patients diagnosed with COVID-19 by RT-PCR. We determined the prevalence of bacterial superinfection and its factors associated with crude and adjusted prevalence ratios by a generalized linear model. The prevalence of superinfection was 49.6%, with 16 agents identified, the most frequent were Klebsiella (pneumoniae and oxytoca) and Staphylococcus aureus. In the multivariate adjustment, the variables with the strongest association with bacterial superinfection were lung disease, encephalopathy, mechanical ventilation, hospital stay, and steroid treatment.
>
> A high prevalence of bacterial superinfections, a high number of agents, and multiple associated factors were found. Among these stood out comorbidities, complications, days of hospitalization, mechanical ventilation, and steroid treatment. These results are vital to identifying priority clinical groups, improving the care of simultaneous infections with COVID-19 in people with the risk factors exposed in the population studied, and identifying bacteria of public health interest."

Other Infectious Diseases

News in Brief

Moderna has started testing its mRNA quadrivalent seasonal flu vaccine; the company wants to develop a respiratory vaccine that combines influenza, a COVID-19 variant booster, and RSV (Moderna).

"Since the beginning of the year, Ituri province in northeastern Democratic Republic of the Congo (DRC) has reported a total of 117 suspected cases of bubonic and pulmonary plague and 13 deaths" (ONT).

Want to wow your friends with medical history knowledge? "How a medieval city dealing with the black death invented quarantine" (NPR). Or you could also read the summary on quarantine with a section on history, from NMCP COVID-19 Lit Report #12 from May 2020 (with sources!).

Peer-Reviewed Articles

Clin Infect Dis: Incidence of Respiratory Syncytial Virus Infection among Hospitalized Adults, 2017-2020 (09 July 2021)

> "Background: Respiratory syncytial virus (RSV) infection causes acute respiratory illness and triggers exacerbations of cardiopulmonary disease. Estimates of RSV incidence in hospitalized adults range widely, and few data exist on incidence in adults with comorbidities that increase the risk of severe disease. We conducted a prospective, population-based, surveillance study to estimate incidence of RSV hospitalization among adults overall and those with specific comorbidities.
>
> Methods: Hospitalized adults ≥18 years residing in the surveillance area with ≥2 ARI symptoms or exacerbation of underlying cardiopulmonary disease were screened for eligibility during the 2017-2018, 2018-2019, and 2019-2020 RSV seasons in three hospital systems in Rochester, NY and New York City. Respiratory specimens were tested for RSV using PCR assays. RSV incidence per 100,000 was adjusted by market share.
>
> Results: During three winter seasons a combination of active and passive surveillance identified 1,099 adults hospitalized with RSV at three medical centers. Annual incidence during three seasons ranged from 44.2-58.9/100,000. Age-group specific incidence ranged from 7.7-11.9/100,000, 33.5-57.5/100,000, and 136.9-255.6/100,000 in patients 18-49, 50-64, and >65-years of age, respectively. Incidence rates in patients with chronic obstructive pulmonary disease, coronary artery disease, and congestive heart failure were 3-13, 4-7, 4-33 times the incidence in patients without these conditions.
>
> Conclusions: We found a high burden of RSV hospitalization in this large prospective study. Notable was the high incidence of RSV hospitalization among older patients and those with cardiac conditions. These data confirm the need for effective vaccines to prevent RSV infection in older and vulnerable adults."

Lancet Planet Health: Projecting the risk of mosquito-borne diseases in a warmer and more populated world: a multi-model, multi-scenario intercomparison modelling study (01 July 2021)

> "Background: Mosquito-borne diseases are expanding their range, and re-emerging in areas where they had subsided for decades. The extent to which climate change influences the transmission suitability and population at risk of mosquito-borne diseases across different altitudes and population densities has not been investigated. The aim of this study was to quantify the extent to which climate change will influence the length of the transmission season and estimate the population at risk of mosquito-borne diseases in the future, given different population densities across an altitudinal gradient.
>
> Methods: Using a multi-model multi-scenario framework, we estimated changes in the length of the transmission season and global population at risk of malaria and dengue for different altitudes and population densities for the period 1951-99. We generated projections from six mosquito-borne disease models, driven by four global circulation models, using four representative concentration pathways, and three shared socioeconomic pathways.
>
> Findings: We show that malaria suitability will increase by 1·6 additional months (mean 0·5, SE 0·03) in tropical highlands in the African region, the Eastern Mediterranean region, and the region of the Americas. Dengue suitability will increase in lowlands in the Western Pacific region and the Eastern Mediterranean region by 4·0 additional months (mean 1·7, SE 0·2). Increases in the climatic suitability of both diseases will be greater in rural areas than in urban areas. The epidemic belt for both diseases will expand towards temperate areas. The population at risk of both diseases might increase by up to 4·7 additional billion people by 2070 relative to 1970-99, particularly in lowlands and urban areas.
>
> Interpretation: Rising global mean temperature will increase the climatic suitability of both diseases particularly in already endemic areas. The predicted expansion towards higher altitudes and temperate regions suggests that outbreaks can occur in areas where people might be immunologically naive and public health systems unprepared. The population at risk of malaria and dengue will be higher in densely populated urban areas in the WHO African region, South-East Asia region, and the region of the Americas, although we did not account for urban-heat island effects, which can further alter the risk of disease transmission."

Statistics

Global
16 JUL 2021: 189,074,478 confirmed cases and 4,069,219 deaths

United States top 5 states by cases

	TOTAL US	CA	TX	FL	NY	IL
Cases	33,978,140	3,846,540	3,032,750	2,404,895	2,123,452	1,399,270
Deaths	608,410	64,043	52,763	38,157	53,759	25,783

JHU CSSE as of 1000 EDT 16 July 2021

Virginia	Total (state)	Chesapeake	Hampton	Newport News	Norfolk	Portsmouth	Suffolk	Virginia Beach
Cases	684,499	21,439	10,797	14,481	18,155	9,264	8,055	36,714
Hospitalizations	30,936	1,049	463	530	1,057	702	479	1,743
Deaths	11,477	311	182	240	274	205	191	419

VA DOH as of 1000 EDT 16 July 2021